National Institute of Environmental Health Sciences

Superfund Research Program

Research Brief 225

Release Date: 09/04/13

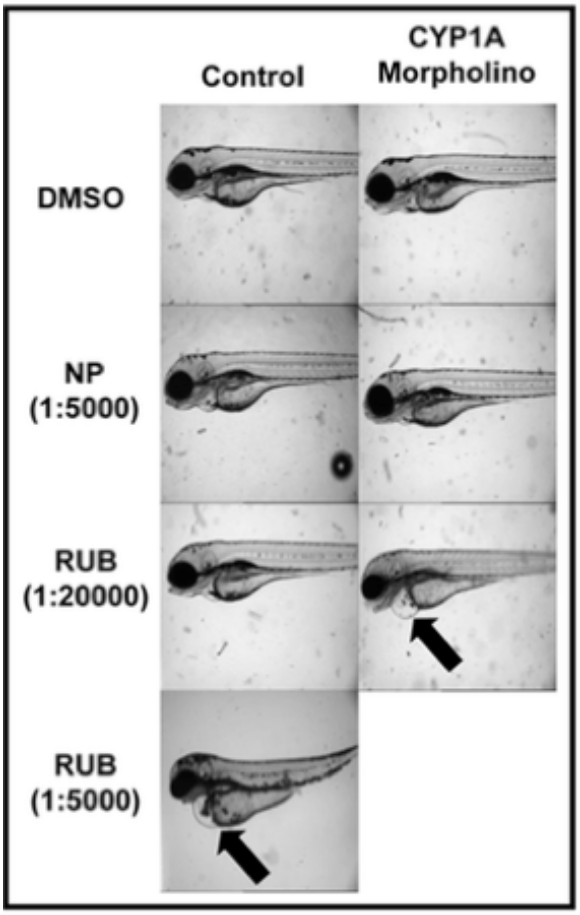
Commercial Paper and Rubber Products Contain Activators of the Aryl Hydrocarbon Receptor

Common commercial and consumer products, including newspapers and rubber bands, contain chemicals that are recognized by the body as toxins, according to a collaborative study by researchers at the Duke University and University of California, Davis Superfund Research Program (SRP) Centers. Solvents extracted from everyday rubber and paper products were shown to activate the aryl hydrocarbon receptor (AhR), which can potentially produce a wide variety of harmful effects in the body.

Dioxins, particularly 2, 3, 7, 8- Tetrachlorodibenzo-p-dioxin (TCDD), and related dioxin-like chemicals are widespread environmental contaminants that produce an assortment of toxic and biological effects, including reproductive and developmental problems, damage to the immune system, cancer, and endocrine disruption. Most biological effects related to dioxin-like chemicals are mediated by the AhR, a protein involved in the regulation of various biological responses and a regulator of enzymes that metabolize chemicals in the body. Although most dioxin-like chemicals are structurally related, recent studies have shown that the AhR will bind to a wide variety of structures, many of which can produce similar health effects.

During an analysis of food products for AhR activators, the accidental use of a rubber cap liner instead of a Teflon cap on vials containing the organic solvent dimethylsulfoxide (DMSO) revealed that chemicals extracted from the rubber cap liner could stimulate AhR DNA binding, while the Teflon-capped vials showed no activation. Based on this finding, the researchers wanted to examine how widespread AhR activators were in commercial and consumer products.

Researchers extracted chemicals from paper, rubber, and plastic products and measured whether they could stimulate AhR DNA binding and/or AhR-dependent gene expression in cultured cell lines, zebrafish embryos, and samples of human skin. They demonstrated that chemicals from the rubber and paper product extracts can bind to the AhR, stimulate AhR DNA binding, and induce AhR-dependent gene expression in cell lines. Solvent extracts of rubber products also caused AhR-dependent developmental toxicity in zebrafish, with zebrafish embryos exposed to rubber extracts exhibiting substantial developmental malformations, including severe deformities in the lower jaw, accumulation of fluid in the brain and near the heart, and cell death in tissues.



Zebrafish embryos were exposed to varying concentrations of newspaper (NP) and rubber (RUB). Deformities in zebrafish were seen with the addition of RUB at the 1:5000 dilution, but not at the lower, 1:20,000 dilution. To determine if chemicals metabolized through the AhR pathway contribute to the toxic effects in zebrafish, embryos were injected with a morpholino to inhibit the metabolic enzyme Cytochrome P450, subfamily A (CYP1A), an enzyme that degrades some AhR-activating chemicals. The deformities seen at a lower RUB concentration, 1:20,000 dilution, with CYP1A morpholino, likely resulted from a decrease in CYP1A-dependent degradation of the chemical(s) responsible for the adverse effects. This, along with other tests performed in the study, show that chemicals present in these extracts can induce AhR-dependent toxicity.

According to the authors, since these commercial products and consumer products contain chemicals with significant AhR binding activity, they may also produce endocrine disrupting effects in exposed animals. They demonstrated that rubber product extracts could stimulate estrogen receptor (ER)-dependent gene expression. While endocrine disrupting chemicals have been identified from a number of environmental sources, most studies focus on identification of known endocrine disruptors, rather than assessing the overall activity of an extract then identifying the responsible chemicals.

The study tested for ER and AhR activity in the chemical extracts and did not look for specific known ER or AhR active chemicals. Although they know now that there are ER- and AhR- active chemicals in the extracts, they do not know yet exactly what the chemicals are, just that they are widely found in these everyday products. Ongoing studies are currently attempting to identify the responsible chemicals.

The study also suggests that AhR- and ER-active chemicals present in rubber and paper products can complicate experimental study by contributing dioxin- and estrogen-like chemicals/activity to sample or sample extracts that come in contact with these materials. Accordingly, the authors suggest that background levels of extractable AhR and ER active chemicals must be determined in sample collection and processing materials in experiments using appropriate method blanks.

For more information, contact

Michael S. Denison, Ph.D.
Department of Environmental Toxicology
University of California,
One Shields Ave.
Davis, CA 95616
Phone: 530-752-3879
Email: msdenison@ucdavis.edu

Richard T. Di Giulio, Ph.D.
Duke University Nicholas School of the Environment
346B LSRC
Box 90328
Durham, NC 27708
Phone: 919-613-8024
Email: richd@duke.edu

To learn more about this research, please refer to the following source:

Zhao B, Bohonowych JE, Timme-Laragy A, Jung D, Affatato AA, Rice RH, Di Giulio RT, Denison MS. 2013. Common commercial and consumer products contain activators of the aryl hydrocarbon (dioxin) receptor. PloS One 8(2): e56860. doi: 10.1371/journal.pone.0056860